

## REMARKS

### I. Introduction

In response to the Office Action dated March 25, 2003, claims 7, 12, 13, 22, 23, 54, 63, 67 and 68, and claims 1, 11, 14, 17, 19-21, 34, 41, 51, 58-60, 66 and 71 have been amended. Claims 1-6, 8-9, 11, 14, 17, 19-21, 25-52, 54, 58-62, 64-66 and 71 remain in the application. Reconsideration of the application, as amended, is requested.

### II. Claim Amendments

Applicants' attorney has made amendments to the claims as indicated above. These amendments were made solely for the purpose of clarifying the language of the claims, and were not required for patentability or to distinguish the claims over the prior art. The amendments do not introduce new matter and their entry is respectfully requested. Support for these amendments can be found in the application as originally filed as noted below.

The amendment to claims 1, 21, 41, 51, and 58 to incorporate the definition of "insulin analog" can be found at page 4, lines 24-27. Because claim terms are interpreted in light of the specification and this is the same definition provided in the specification, this amendment does not alter the scope of these claims.

The amendment to claims 1, 21, 41, 51, 58 and 59 to more clearly define the term "insulin-related peptide" merely incorporates the language of dependent claims such as original claim 7 and is consistent with the definition of this term provided in the specification at page 5, line 26, to page 6, line 9.

Claims 1, 51, 58 and 59 have been amended to recite a non-ionic surfactant that is a block copolymer of propylene oxide and ethylene oxide, as supported by original dependent claims such as claims 12 and 13.

Claims 11, 14, 17 and 66 have been amended to clarify that the composition is a liquid where the recited ingredients are present in quantities expressed in mg/ml.

Claim 19 has been amended to clarify the language as suggested by the Examiner.

Claims 20 and 71 have been amended to clarify that what is meant by two or more compounds of a recited agents refers to an additional compound over the one recited in the parent claim, as suggested by the Examiner.

Claim 21 has been amended to recite the optional presence of a carrier, as suggested by the Examiner.

Claim 34 has been amended to correct the reference to a preceding claim given the cancellation of claim 12.

Claim 60 has been amended to correct the antecedent basis.

### III. Non-Art Rejections

On page (2) of the Office Action, claims 1-7, 9-14, 19-23, 25, 59-63, 65-68, and 71 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Applicants have amended the claims as indicated above to overcome this rejection.

Although the Examiner indicated that the term "L-783,281" recited in claim 61 should be accompanied by the chemical name this term represents, Applicants have not amended this claim because "L-783,281" is the name by which this molecule is known in the art. Applicants respectfully refer the Examiner to the abstract submitted herewith of Zhang et al., 1999, "Discovery of a small molecule insulin mimetic with antidiabetic activity in mice," Science 284(5416):886. This abstract indicates that L-783,281 is the name by which this molecule has been known in the art since prior to the filing date of the present application. Should the Examiner be aware of a more appropriate chemical name for this molecule, Applicants will gladly amend claim 61 accordingly.

### IV. Prior Art Rejections

On page (4) of the Office Action, claims 1, 59, and 71 were rejected under 35 U.S.C. §103 as being unpatentable over Rieveley, U.S. Patent No. 6,153,632 (Rieveley). On page (5) of the Office Action, claims 1, 59, and 71 are rejected under 35 U.S.C. §103 as being unpatentable over Knudsen, U.S. Patent No. 6,268,343 (Knudsen) in view of either (a) Smith, WO 98/57636 (Smith) or Rieveley. On page (7) of the Office Action, claims 1, 59, and 71 were rejected under 35 U.S.C. §103 as being unpatentable over Tomas, WO 96/02270 (Tomas) in view of either Smith or Rieveley. Also on page (7) of the Office Action, claims 1, 59, and 71 were rejected under 35 U.S.C. §103 as being unpatentable over Rink, WO 92/20366 (Rink) in view of either Smith or Rieveley. On page (8) of the Office Action, claims 1, 59, and 71 were rejected under 35 U.S.C. §103 as being unpatentable

over Clark, U.S. Patent No. 5,783,556 (Clark) in view of either Smith or Rieveley. Also on page (8) of the Office Action, claims 1, 59, and 71 were rejected under 35 U.S.C. §103 as being unpatentable over Cooper, U.S. Patent No. 5,641,744 (Cooper) in view of either Smith or Rieveley. On page (9) of the Office Action, claims 1, 59, and 71 were rejected under 35 U.S.C. §103 as being unpatentable over Froesch, U.S. Patent No. 4,988,675 (Froesch) in view of either Smith or Rieveley. Also on page (9) of the Office Action, claims 1, 59, and 71 were rejected under 35 U.S.C. §103 as being unpatentable over Chance, U.S. Patent No. 4,652,548 (Chance) in view of either Smith or Rieveley. On page (10) of the Office Action, claims 1, 59, and 71 were rejected under 35 U.S.C. §103 as being unpatentable over L'Italien, U.S. Patent No. 6,136,784 (L'Italien) in view of either Smith or Rieveley. Also on page (10) of the Office Action, claims 1, 59, and 71 were rejected under 35 U.S.C. §103 as being unpatentable over Habener, U.S. Patent No. 5,958,909 (Habener) in view of either Smith or Rieveley.

Each of the rejected claims, claims 1, 59 and 71, has been amended to incorporate all of the limitations of non-rejected dependent claims. Accordingly, the rejection of these claims is now moot.

Even prior to the amendments to the claims, however, Applicants note that the cited references do not teach or suggest the combination of elements recited in Applicants' independent claims. For the record, Applicants wish to clarify that Applicants' argument does not rely on the fact that a single reference fails to teach all of the elements of the claims (which is true, but not relevant to the rejection based on obviousness). Instead, Applicants respectfully maintain that none of the cited references teach or suggest, when taken alone or in combination, the combination of elements recited in the claims.

As noted by the Examiner in the final full sentence of page 5 of the Office Action and again on page 6, the relevant issue is whether motivation to combine the compounds can be found in the prior art. Although the Examiner states that such motivation exists in the present case, the reasoning in support of this assertion is not apparent. The Examiner notes at page 6 of the Office Action that one would expect an additive effect when combining compounds, but also notes that this is not always the case.

Applicants maintain that, were such an additive effect obvious to the skilled artisan, surely the combination would have been suggested in at least one of the cited references to the extent that

they suggest additional agents for co-administration. Instead, the cited references teach away from the claimed combination because the references do explicitly suggest combination with additional anti-diabetic agents, but they direct one to select a conventional hypoglycemic agent (sulfonylurea, biguanide or alpha-glucosidase inhibitor) as the third ingredient.

Moreover, the various elements of Applicants' claimed invention together provide operational advantages over Rieveley, Knudsen, Smith, Tomas, Rink, Clark, Cooper, Froesch, Chance, L'Italien, and Habener. In addition, Applicants' invention solves problems not recognized by Rieveley, Knudsen, Smith, Tomas, Rink, Clark, Cooper, Froesch, Chance, L'Italien, and Habener. As discussed at page 5, lines 15-20, of the specification, the claimed invention provides thermally stable compositions. The creation of safe domains by use of a non-ionic surfactant protects the relatively thermally unstable insulin-related peptides, enabling effective co-administration of the combination of agents.

Thus, Applicants submit that the independent claims are allowable over Rieveley, Knudsen, Smith, Tomas, Rink, Clark, Cooper, Froesch, Chance, L'Italien, and Habener. Further, the dependent claims are submitted to be allowable over Rieveley, Knudsen, Smith, Tomas, Rink, Clark, Cooper, Froesch, Chance, L'Italien, and Habener in the same manner, because they are dependent on the independent claims and thus contain all the limitations of the independent claims. In addition, the dependent claims recite additional novel elements not shown by Rieveley, Knudsen, Smith, Tomas, Rink, Clark, Cooper, Froesch, Chance, L'Italien, and Habener.

**V. Conclusion**

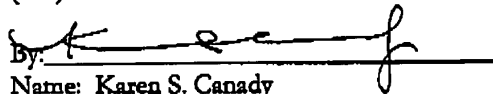
In view of the above, it is submitted that this application is now in good order for allowance and such allowance is respectfully solicited. Should the Examiner believe minor matters still remain that can be resolved in a telephone interview, the Examiner is urged to call Applicants' undersigned attorney.

Respectfully submitted,

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